Claims

1. An isolated nucleic acid molecule selected from the group consisting of

(a) nucleic acid molecules that code for the amino acid sequence of SEQ ID NO:2,

(b) allelic variants of (a), wherein the allelic variants exclude SEQ ID NO:3 and SEQ ID NO:5, and

(c) complements of (a) or (b).

2. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule codes for SEQ ID NO:2.

3. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid comprises the nucleotide sequence of SEQ ID NO:1.

4. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid comprises the coding region of SEQ ID NO:1.

5. The isolated nucleic acid molecule of claim 1, wherein the allelic variants are nucleic acid molecules that code for an amino acid sequence selected from the group consisting of SEQ ID NO:23, SEQ ID NO:25 and SEQ ID NO:27.

6. The isolated nucleic acid molecule of claim 5, wherein the allelic variant codes for SEQ ID NO:23.

7. The isolated nucleic acid molecule of claim 5, wherein the allelic variant codes for SEQ ID NO:25.

8. The isolated nucleic acid molecule of claim 5, wherein the allelic variant codes for SEQ ID NO:27.

9. The isolated nucleic acid molecule of claim 5, wherein the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:22, SEQ

ID NO:24 and SEQ ID NO:26.

10. The isolated nucleic acid molecule of claim 9, wherein the nucleotide sequence comprises SEQ ID NO:22.

11. The isolated nucleic acid molecule of claim 9, wherein the nucleotide sequence comprises SEQ ID NO:24.

12. The isolated nucleic acid molecule of claim 9, wherein the nucleotide sequence comprises SEQ ID NO:26.

13. The isolated nucleic acid molecule of claim 5, wherein the nucleic acid molecule comprises a coding region of a nucleotide sequence selected from the group consisting of SEQ ID NO:22, SEQ ID NO:24 and SEQ ID NO:26.

14. An isolated P-glycoprotein polypeptide or fragment thereof which comprises at least one amino acid of a dog P-glycoprotein selected from the group consisting of amino acids 25, 192, 197, 212, 288, 329, 532, 696, 1273 and 1355 of SEQ ID NO:2; amino acid 25 of SEQ ID NO:25; and amino acids 25 and 1148 of SEQ ID NO:27.

15. An isolated P-glycoprotein polypeptide or fragment thereof which comprises at least one amino acid of a dog P-glycoprotein selected from the group consisting of amino acids 3, 6, 8, 10, 12, 14-26, 36, 38, 48, 52, 56, 64, 74, 78, 84-92, 94, 96, 98, 99, 101, 103, 104, 106, 108, 112, 115, 147, 187, 197, 199, 233, 288, 321, 326, 347, 397, 450, 454, 455, 467, 472, 520, 633, 637, 643, 644, 650, 657, 658, 661, 666, 667, 674-677, 679, 685, 689, 691, 693, 694, 703, 707, 717, 731, 736, 740, 744, 745, 756, 759, 763, 853, 914, 920, 942, 943, 946, 968-970, 972, 974, 983, 1005, 1010, 1017, 1025, 1026, 1029, 1040, 1095, 1098, 1105, 1144, 1148, 1149, 1158, 1162, 1165, 1168, 1170, 1252 and 1279 of SEQ ID NO:2; and amino acid 329 of SEQ ID NO:27, wherein the P-glycoprotein is identical to a human P-glycoprotein except for the at least one amino acid of a dog P-glycoprotein.

16. The isolated P-glycoprotein polypeptide or fragment thereof of claim 15, wherein the

human P-glycoprotein is selected from the group of SEQ ID NO:7 and SEQ ID NO:8.

17. The isolated P-glycoprotein polypeptide or fragment thereof of any of claims 14-16, wherein the amino acid sequence of the polypeptide or fragment thereof is an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, fragments of SEQ ID NO:2, fragments of SEQ ID NO:23, fragments of SEQ ID NO:25 and fragments of SEQ ID NO:27.

18. An isolated nucleic acid molecule which encodes the isolated P-glycoprotein polypeptide or fragment thereof of any of claims 14-17.

19. An expression vector comprising the isolated nucleic acid molecule of claim 1 operably linked to a promoter.

20. An expression vector comprising the isolated nucleic acid molecule of claim 18 operably linked to a promoter.

21. A host cell transformed or transfected with the expression vector of claim 19.

22. A host cell transformed or transfected with the expression vector of claim 20.

23. An agent which selectively binds the isolated polypeptide of claim 14.

24. The method of claim 23, wherein the agent does not bind a human or dog P-glycoprotein.

25. The agent of claim 23, wherein the agent is a polypeptide.

26. The agent of claim 25, wherein the polypeptide is selected from the group consisting of monoclonal antibodies, polyclonal antibodies, Fab antibody fragments, $F(ab)_2$ antibody fragments and antibody fragments including a CDR3 region.

27. An agent which selectively binds the isolated nucleic acid molecule of claim 1 or claim 18.

28. The agent of claim 27, wherein the agent is an antisense nucleic acid which selectively binds to the isolated nucleic acid molecule.

29. A method for predicting the bioavailability of a compound, comprising

measuring the transmembrane transport of a test compound by a first P-glycoprotein,

comparing the transmembrane transport of the test compound by the first P-glycoprotein and a second P-glycoprotein to predict the bioavailability of the test compound, wherein the relative amount or rate of transport by the first P-glycoprotein and the second P-glycoprotein is predictive of bioavailability of the test compound.

30. The method of claim 29, wherein the first P-glycoprotein is selected from the group consisting of dog P-glycoproteins and primate P-glycoproteins.

31. The method of claim 29, wherein the first P-glycoprotein is the polypeptide of claims 14-17.

32. The method of claim 29, wherein the second P-glycoprotein is a human P-glycoprotein.

33. A method for inhibiting P-glycoprotein transporter activity in a mammalian cell comprising

contacting the mammalian cell with an amount of the agent of claim 27 effective to inhibit P-glycoprotein transporter activity in the mammalian cell.

34. A method for increasing bioavailability of a drug in a subject comprising

administering to a subject in need of such treatment the agent of claim 27 in an amount effective to increasing bioavailability of a drug.

35. The method of claim 34, wherein the inhibitor is administered prior to administering

the drug.

36. The method of claim 34, wherein the inhibitor is administered concurrently with the drug.

37. A method for increasing P-glycoprotein transporter activity in a cell comprising

contacting the cell with a molecule selected from the group consisting of the nucleic acid molecule of claim 1 and the nucleic acid molecule of claim 18, in an amount effective to increase P-glycoprotein transporter activity in the cell.

38. A method for identifying lead compounds for a pharmacological agent useful in the treatment of disease associated with P-glycoprotein transporter activity comprising

providing a cell or other membrane-encapsulated space comprising a P-glycoprotein as claimed in claim 14 or 15;

contacting the cell or other membrane-encapsulated space with a candidate pharmacological agent under conditions which, in the absence of the candidate pharmacological agent, cause a first amount of P-glycoprotein transporter activity;

determining a second amount of P-glycoprotein transporter activity as a measure of the effect of the pharmacological agent on the P-glycoprotein transporter activity, wherein a second amount of P-glycoprotein transporter activity which is less than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces P-glycoprotein transporter activity and wherein a second amount of P-glycoprotein transporter activity which is greater than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases P-glycoprotein transporter activity.

39. The method of claim 38, further comprising the step of loading the cell or other membrane-encapsulated space with a detectable compound, wherein the compound is detected as a measure of the P-glycoprotein transporter activity.

40. A method for identifying compounds which selectively bind a P-glycoprotein comprising,

contacting the P-glycoprotein claimed in claim 14 or 15 with a compound, determining the binding of the compound to the P-glycoprotein.

41. The method of claim 40 further comprising determining the effect of the compound on the P-glycoprotein transporter activity of the P-glycoprotein.

42. The method of claim 40 further comprising determining the effect of the compound on the ATPase activity of the P-glycoprotein.

43. A method for determining ATPase activity of a P-glycoprotein comprising

contacting the host cell of claim 20 or 22, or a membrane fraction thereof, with a test drug, and

measuring ATPase activity of the P-glycoprotein.

44. The method of claim 43, wherein the step of measuring ATPase activity is performed at least twice at different times.

45. A method for determining transmembrane transport of a compound by a P-glycoprotein, comprising

contacting the host cell of claim 20 or 22, or a membrane fraction thereof, with a test drug, and

measuring transport of the test drug under sink conditions in at least one direction of transport selected from the group consisting of the apical to basolateral direction and the basolateral to apical direction.

46. The method of claim 45, wherein the step of measuring transport of the test drug is performed at least twice at different times.